REMARKS

Claims 46, 54-77, and 80-107 are now pending in the case, new claims 102-107 having been added by the above amendment. Support for the new claims can be found in the specification, for example, at page 4, lines 1-23. No new matter has been added.

The invention

Until recently, chlorofluorocarbons (CFCs) were widely used as propellants in pressurized metered dose inhalers (pMDI) for delivery of medicaments to the airways. CFCs are organic compounds. Where the medicament to be delivered by pMDI was not soluble in organic media such as liquified CFC, it was typically formulated as a suspension of fine powder particles in the liquified propellant. Surfactants were commonly included in order to aid dispersion of the medicament particles in the CFC propellant; without such surfactants, the particles would tend to aggregate. According to page 97, col.1, lines 19-23, of McDonald et al., International Journal of Pharmaceutics 201:89-107, 2001 (attached as Appendix A), the surfactants used with "currently licensed" CFC metered dose inhalers are oleic acid, sorbitan triethanoleate and soya derived lecithin.

Due to environmental concerns, CFCs are now being replaced by a new generation of propellants: hydrofluoroalkane (HFA) propellants. As explained in the present application as well as in McDonald et al., the surfactants commonly used with CFC formulations are not necessarily suitable for use with HFAs. Applicants have found that certain classes of surfactants are particularly suitable for dispersing fine particles of medicament in the new generation of propellant. The present claims are drawn to formulations containing an HFA, a medicament, and an alkyl saccharide surfactant, and method of using such formulations in therapy.

Provisional obviousness-type double patenting

All of the claims were provisionally rejected for obviousness-type double patenting over co-pending USSN 08/624,504. Applicants will file an appropriate terminal disclaimer once the claims are otherwise deemed allowable.

35 USC §103(a)

All of the claims were rejected as obvious over WO 91/11495 in view of Neale et al., Sequeira et al., and Meezan et al. According to the Examiner,

> The difference between the prior art and the claimed invention is that the prior art does not expressly disclose the combination of fluorocarbons, medicine and alkyl saccharides in a pharmaceutical aerosol formulation. However, the prior art amply suggests the same as it is known to produce pharmaceutical aerosols containing fluorocarbons and surfactants and that alkyl saccharides are suitable for use as surfactants in medical aerosols. As such, it would have been well within the skill of and one of ordinary skill in the art would have been motivated to modify the prior art as above with the expectation that the medical aerosol would exhibit increased bioavailability of the administered medicine(s) and would be suitable for administration of a broader range of medicines.

Applicants respectfully traverse. The claims are limited to formulations (and methods of use thereof) comprising HFAs, medicaments, and alkyl saccharides. The first three references cited by the Examiner (WO 91/11495, Neale et al., and Sequeira et al.) discuss various formulations containing HFAs, medicaments, and surfactants. However, as recognized by the Examiner, none discloses that the surfactant can be an alkyl saccharide, as required by the present claims. Of the four references cited, only one (Meezan) even mentions alkyl saccharides (termed "alkyl glycosides" in Meezan).

As noted by the Examiner, Meezan also does not disclose the claimed combination. The alkyl saccharide-containing formulations utilized in Meezan's examples are in formulated in saline (i.e., aqueous solution), rather than a non-aqueous, organic medium such as HFA or CFC. Alkyl saccharides are employed in Meezan's examples not to improve dispersion of particles (indeed, there apparently are no particles in Meezan's aqueous formulations), but rather to enhance absorption into the bloodstream of a medicament dissolved in aqueous solution. In fact, Meezan teaches at col. 4, lines 34-36, that the supposed absorption-enhancing effect of alkyl glycosides can be obtained even if the medicament and the alkyl glycoside are not present in the same formulation, but rather are administered sequentially. This makes it clear that Meezan utilizes alkyl glycosides for a purpose unrelated to improving the physical characteristics of the formulation. Furthermore, the experimental examples in Meezan are limited to delivery of aqueous solution in drop form, into the eyes of subjects. Meezan does not teach that alkyl

saccharides would serve any purpose at all (absorption enhancing or otherwise) in a non-aqueous, propellant-based formulation. One cannot extrapolate results obtained with ocular delivery of a simple aqueous solution in order to predict success with an entirely different, and more complex, formulation utilized in an entirely different mode of delivery. Thus, Meezan provides neither the motivation nor the expectation of success necessary to underpin an obviousness rejection under US law.

Nor would one reading the other three cited references look to Meezan (which says nothing about surfactants useful in propellant-based formulations, much less HFA formulations) for guidance in selecting a surfactant appropriate for use in an HFA formulation. As discussed in McDonald et al. (Appendix A) at page 97, even if a given surfactant has been proven to be useful with the non-aqueous medium CFC, one can't assume it will also be useful with the non-aqueous medium HFA, as their physical and chemical properties are so different. Much less could one select a surfactant for HFA formulations based on its use for unrelated purposes in the aqueous solutions of Meezan. There is neither motivation nor expectation of success to be found anywhere in the cited art. The rejection is therefore unwarranted, and withdrawal is respectfully requested.

Applicant asks that all claims be allowed. Enclosed is a $108.00 check for excess claim fees and a $920.00 check for the Petition for Extension of Time fee. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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